DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

M2924n

AUG 27 1999

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

VIA FEDERAL EXPRESS

WARNING LETTER

Mr. K.S. Ratra
Director RFB Latex Limited
Surya Plaza, First Floor
A-33, New Friends Colony
New Delhi-110 025
India

Dear Mr. Ratra:

During an inspection of your firm located in Noida, 201305, India on July 1, 1999, our investigator determined that your firm manufactures sterile latex surgical and examination gloves. These are devices as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as listed below. Your response, dated July 10, 1999, to the investigator's findings was also reviewed. Comments on your response follow each observation.

1. Failure to, where the results of a process cannot be fully verified by subsequent inspection and test, validate the process with a high degree of assurance and approve that process according to established procedures, as required by 21 CFR 820.75(a). For example, the validation report shows that the validation project was actually a study to determine the best sealing parameters. The validation study did not show that the process is reproducible and consistent. There is no installation qualification for packaging machine

   Your response is not adequate. Revalidation of one packaging machine [redacted] is underway, and validation of the unqualified packaging machine [redacted] is in progress. Completion of both validations is not expected until [redacted]

2. Failure to develop, conduct, control, and monitor production processes to ensure that a device conforms to its specifications, and to establish and maintain process control procedures that describe any process controls necessary to ensure conformance to specifications, as

required by 21 CFR 820.70(a). For example, there are no biological indicators (BI) included with the routine [redacted] sterilization of surgical and examination latex gloves.

Your response may be adequate. The system of testing BIs for routine sterilization has been incorporated in Standard Operating Procedure (SOP) No. QAP/4 (paragraph 6.5.2) and a [redacted]

The relevant BI segment of the SOP has been implemented, and the [redacted] is enclosed with the response.

3. Failure to maintain a device master record prepared, dated, and signed by a designated individual for each type of device, including or referring to production process specifications including appropriate equipment specifications, production methods, production procedures, and production environmental specifications, as required by 21 CFR 820.181(b). For example:

   a. The parameters determined during the validation of the sealing machine [redacted] were not included in the device master record after approval.

   b. The procedure titled "IN-PROCESS INSPECTION AND TESTING" requires the wallet packing and sealing machines, [redacted] to be set and maintained as per "Approved validated parameters". However, the parameters are not documented in any procedure.

Your response is not adequate. The revised page to the device master record, including 10.6 Process Control, states Process Control is exercised as per QAP/4.9-"Process Control". Following that is a page of the Procedure Manual, Section 7.0 Sealing of Wallets. This section includes the parameters for the seals of the wallets performed on the sealing machines. The validation of the sealing machines will not be completed until [redacted] Confirmation of the sealing parameters is not possible before [redacted] Additional information will be needed to determine the accuracy of the validation parameters.

4. Failure to investigate the cause of non-conformities relating to product, processes, and the quality system, as required by 21 CFR 820.100(a)(2). For example, [redacted] product were rejected during the inspection of the package (wallet) seal from [redacted] There was no evaluation and investigation of the cause of the incomplete seal creating the non-conformances.

Your response may be adequate. New Procedure No. QAP/4.14 pertaining to corrective and preventive action for non-conforming products is included with the response. The response states training was organized regarding this procedure for the quality control staff. There is no documentation supporting the scheduling of completion of training for the quality control staff.

5. Failure to establish and maintain procedures to control all documents required by this part with procedures that provide for review and approval of changes to documents by an individual(s) in the same function or organization that performed the original review and approval, unless specifically designated otherwise, as required by 21 CFR 820.40(b). For example, the approved validated parameters for sealing of the glove "wallets" were changed without following the change control procedure QAP/4.5. The log book for the sealing machines shows operating parameters out of specification. The parameters were changed on [redacted] without any documented justification or approval.

   Your response is not adequate. Included with the response are copies of the established procedure QAP/4.9 including the parameters changed [redacted] without prior authorization, the Document Change Control Request approved [redacted] and the Reasons for the Change as Annex 2. The reasons for the change were that the original parameters could not be [redacted] Therefore, the machines needed validation for one, and revalidation for the other to support the new parameters. Although the Change Control Request was approved by management on [redacted] the validation and revalidation will not be completed until [redacted] Therefore, it is unknown whether the new parameters are adequate and supportable.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the form FDA 483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the Food and Drug Administration. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts.

Given the serious nature of these violations of the Act, all devices manufactured by RFB Latex Limited, 24 NEPZ, Distt. Gautam Budh, Nagar, Noida 201305, India may be detained without physical examination upon entry into the United States (U.S.) until these violations are corrected.

In order to remove the devices from this detention, it will be necessary for you to provide the additional requested documentation to the charges in this Warning Letter for our review. After we notify you that the response is adequate, it will be your responsibility to schedule an inspection of your facility. As soon as the inspection has taken place, and the implementation of your corrections has been verified, your products may resume entry into this country.

Please notify this office in writing of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter.

If documentation is not in English, please provide an English translation to facilitate our review.

Your response should be sent to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement I, General Surgery Devices Branch, 2098 Gaither Road, Rockville, Maryland 20850, to the attention of Carol Shirk.

Sincerely yours,

Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health